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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,277	03/01/2002	Graeme Cox	032505-010	6035

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,277	COX ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of invention group I in Paper filed September 9, 2003 is acknowledged. The traversal is on the ground(s) that the two groups are in the same claims. This is not found persuasive because the two groups are directed to separated and distinct subject matters as discussed in the prior office action. Particularly, they involve structurally distinct compounds, search of all those compounds encompassed by the claimed inventions would be an undue burden.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election with traverse of HMA as the elected compounds in Paper filed December 15, 2003 is acknowledged. The traversal is on the ground(s) that DMA and HMA are both closely related derivative of amiloride. The traverse is persuasive and the species election requirement with respect to compound is herein withdrawn.

The claims have been examined insofar as they read on elected invention.

Claim Rejections 35 U.S.C. 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7, 12-17, 30-32, 37-39, 44,45, 50-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite "amiloride analogue," which is

defined in the specification as "any amiloride molecule which exhibits an addition, deletion or substitution." Therefore, the "amiloride analogue" herein encompasses unlimited number of compounds, and obviously, majority of the compounds are not known to the art. the application fails to provide proper written description in two aspects. First, it does not provide written description as to how to make or use those "amiloride analogue;" second, it does not provide written description as to how and why the bioactivity of the particular amiloride compounds, HMA and DMA, would be carried over to any amiloride analogue. As substitution or deletion goes, the properties, including biological properties of a molecule would change. It would not be reasonable to expect a molecule to maintain its biological properties with any substitution or deletion.

1. Claims 1-7, 12-17, 30-32, 37-39, 44,45, 50-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for HMA, DMA or amiloride, does not reasonably provide enablement for any other compounds which may meet the definition of "amiloride analogue." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

4. The claims recite "amiloride analogue," which is defined in the specification as "any amiloride molecule which exhibits an addition, deletion or substitution." Therefore, the "amiloride analogue" herein encompasses unlimited number of compounds, and obviously, majority of the compounds are not known to the art. Applicants fail to provide information allowing skilled artisan to ascertain and make these compounds without undue experimentation. In the instant case, only a limited number of "amiloride analogue" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The instant claims read on all "amiloride analogue", necessitating an exhaustive effort for the embodiments suitable to practice the claimed invention, absent undue experimentation. Further, the claims are not enabled because there is reasonable doubt that all the "amiloride analogue" encompassed herein would be useful for the claimed utility. Note it is not reasonable to expected a molecule to maintain its biological properties with any substitution or deletion.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 22-29 provides for the use of amiloride compounds, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 22-29 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections 35 U.S.C. 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 37-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke (US 5,215,991).

Burke teaches a pharmaceutical composition comprising N,N-hexamethylene amiloride, or N, N-dimethyl amiloride. See the claims. Note it is well settled that the "intended use" of a product or composition will not further limit claims drawn to a product or composition. See, e.g., In re Hack 114 USPQ 161.

Claims Rejections 35 U.S.C. 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-21, 30-36 and 50-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipton (US 5,506,231), in view of Benos et al. and Burke (US 5,215,991).

12. Lipton teaches a method for treating patient infected with HIV comprising administering to the patient a effective amount of Ca+ ion channel antagonist, see the Claims. amiloride is disclosed as a known Ca+ channel antagonist. See table 3 in column 4.

13. Lipton does not teaches expressly the employment of amiloride, or the particular derivatives herein, for treating HIV infected patient.

14. However, Benos teaches that amiloride negates the effect of HIV toxic protein to the cells. See, particularly, the abstract. Burke teaches that amiloride and its analogues as herein recited are known to be similarly useful. See the entire document, particularly, the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use amiloride, or its analogue, such as HMA or DMA, as Ca+ channel antagonist for treating HIV infected patients.

A person of ordinary skill in the art would have been motivated to , to use amiloride, or its analogue, such as HMA or DMA, as Ca+ channel antagonist for treating HIV infected patients because amiloride is particularly known to negate the toxic effect introduced by HIV toxic protein, and the amiloride analogues, HMA and DMA, are known to be similarly useful as amiloride. As to the particular functional limitation, e.g., HIV repliction, note the functional limitations herein do not carry patentable weight since the the ultimate utility as herein claimed, reating HIV infected patient, is obvious to the priro art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (571)272-0632. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9302.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

S. SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang

March 20, 2004